CLAIMS

1. A method for identifying a substance capable of disrupting an interaction between (i) a herpes simplex virus (HSV) ICP34.5 polypeptide or a homologue thereof, or a derivative thereof, and (ii) proliferating cell nuclear antigen (PCNA) or a homologue thereof, or a derivative thereof, which method comprises:

(a) providing an HSV ICP34.5 polypeptide or a homologue thereof, or a derivative thereof, as a first component;

(b) providing PCNA, or a homologue thereof, or a derivatives thereof, as a second component;

(c) contacting the two components with a substance to be tested under conditions that would permit the two components to interact in the absence of the said substance; and

(d) determining whether the said substance disrupts the interaction between the first and second components.

2. A method according to claim 1 wherein the first component is selected from the 63 amino acid C-terminus of ICP34.5 or a derivative thereof, MyD116 and GADD34.

3. A method according to claim 1 ~~or 2~~ further comprising:

(e_1) administering a said substance which has been determined to disrupt the interaction between the first and second components to a mammalian cell; and

(f_1) determining the effect of the said substance on the cell cycle of the said cell.

4. A method according to claim 3, wherein the ability of the said substance to induce cell cycle arrest is determined.

5. A method according to claim 3, wherein the ability of the said substance to induce cell death by apoptosis is determined.

6. A method according to claim 1 ~~or 2~~ further comprising:

(e_2) administering a virus to a cell in the absence of a said substance which has been determined to disrupt the interaction between the first and second components;

(f_2) administering the virus to the cell in the presence of the said substance; and

(g_2) determining if the said substance reduces or abolishes the susceptibility of the cell to viral infection.

7. A substance capable of disrupting an interaction between (i) a herpes simplex virus ICP34.5 polypeptide or a homologue thereof, or a derivative thereof, and (ii) PCNA or a homologue thereof, or a derivative thereof, for use in regulating the cell cycle of a mammalian cell.

8. A substance according to claim 7 for use in inducing growth arrest and/or cell death.

9. A substance according to claim 8 wherein said mammalian cell is a tumour cell.

10. A substance according to claim 7 for use in preventing cell death.

11. A substance according to claim 10 wherein said mammalian cell is a cell of the central or peripheral nervous system.

12. A substance capable of disrupting an interaction between (i) a herpes simplex virus ICP34.5 polypeptide or a homologue thereof, or a derivative thereof, and (ii) PCNA or a homologue thereof, or a derivative thereof, for use in preventing or treating a viral infection.

13. A substance according to claim 12 wherein said viral infection is caused by herpes simplex virus type 1.

14. A method of regulating the cell cycle in a mammalian cell, which method comprises administering to said cell a substance capable of disrupting an interaction between (i) a herpes simplex virus ICP34.5 polypeptide or a homologue thereof, or a derivative thereof, and (ii) PCNA or a homologue thereof, or a derivative thereof.

15. A method according to claim 14 wherein administration of the said substance induces growth arrest and/or cell death.

16. A method according to claim 15 wherein said mammalian cell is a tumour cell.

17. A method according to claim 14 wherein administration of the said substance prevents cell death.

18. A method according to claim 17 wherein said mammalian cell is a cell of the central or peripheral nervous system.

19. A human GADD34 homologue which has the following features:

(i) a molecular mass of approximately 70 kDa as determined by SDS-PAGE;

(ii) a conserved region which is cross-reactive with an anti-ICP34.5 antibody;

(iii) cross-reactive with anti-GADD34 antibodies;

(iv) induced in permissive mammalian cells in response to HSV infection;

(v) not induced in permissive mammalian cells in response to heat shock or UV damage; and

(vi) not induced in non-permissive mammalian cells in response to HSV infection.

20. A homologue according to claim 19 wherein said conserved region has at least 30% homology with the C-terminal 63 amino acid residues of an HSV ICP34.5 polypeptide.

Add B3

Add B4

Add B2